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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,397	09/26/2003	Ronald Rooke	032751-094	2721

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,397	ROOKE, RONALD	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-21,26 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25,27-33 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/969,770.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed January 18, 2005 is acknowledged and entered. Claims 1-38 are pending. Claims 1-21, 26 and 34 remain withdrawn from consideration being drawn to non-elected subject matter. Claims 22-25, 27-33 and new claims 36-38 are under examination.

2. The objection to the specification is withdrawn in view of Applicant's amendment updating the status of related applications. The objection to claim 25 is withdrawn in view of Applicant's amendment correcting a misspelling.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-25, 27-33 and 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 22 and all dependent claims (23-25, 27-33 and 35-38) lack antecedent basis. Claim 22 lacks antecedent basis in itself because the claim refers to "the non-retained E3 region", however, newly amended claim 22 does not have support for this phrase. Prior to the amendment filed January 18, 2005, the claim had proper support. Correction is required.
- Claim 27 recites, "A viral particle comprising the adenoviral vector of claim". There is no further information about the claim from which claim 27 depends, nor is there a period

at the end of the sentence. Correction is required. For purposes of compact prosecution, the Office will interpret claim 27 as dependent from claim 22.

- Claim 37 is unclear for reciting, "said retained E3 sequences encoding a functional 10.4 K protein precedes said retained E3 sequences encoding a functional 14.5 K protein". It appears that Applicant may be referring to a positional limitation when referring to "precedes", however it is not clear. (There is a also a subject-verb agreement grammar problem with "said retained E3 sequences"..."precedes".) Suggested language is, "said retained E3 sequences encoding a functional 10.4 K protein are positioned upstream of the retained E3 sequences encoding a functional 14.5 K protein".

Claim Rejections - 35 USC § 102

4. Claims 22, 25 and 28-30 remain rejected under 35 U.S.C. 102(b) as being anticipated by Bout *et al.* (EP 0707071 A1, herein, "Bout") for reasons of record. Claim 38 is now included in this rejection. Claim 28 is drawn to a limitation of the vector of claim 22, which requires that the retained E3 sequences are placed under the control of a heterologous promoter. This claim is anticipated by Bout, which discloses the use of the heterologous CMV promoter (page 4, lines 49-52). Applicant's arguments have been carefully considered, but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Bout teaches a vector comprising a complete E3 region, while the instant claims are drawn to a vector comprising a modified E3 region that retains only sequences encoding functional 14.5K and 10.4K proteins.

- In response, the claims are not exclusive of other E3 sequences. Claim 22 recites, "wherein said adenoviral vector retains E3 sequences encoding: a functional 14.5K protein and a functional 10.4K protein". This phrase is not limiting the E3 region to only the 14.5 and 10.4 K proteins. The claims still broadly encompass any "modified" E3 region that retains sequences encoding the recited proteins. The "non-retained E3 region" that the amended claim refers to is also non-limiting language. All that is required to meet the limitations of claim 22 is that the vector have a "modified E3" that continues to express 14.5K and 10.4K proteins. The claims do not use language that actually limits the sequences that are present in the vector.

- Applicant argues that the complete E3 region is the only contemplated embodiment of Bout's vectors that include E3. Applicant points to portions of the specification that indicate that the entire E3 region is retained, including working examples containing the wild-type E3 region.

  - In response, the Office notes that Bout does contemplate complete E3 regions being retained, but also contemplates functional regions of E3 being retained (page 3, lines 32-33). An E3 with only functional regions retained is a modified E3. Bout points out which regions are required for reducing host cell responses against infected cells (page 3, lines 1-29) which include the RID complex (10.4K and 14.5K proteins). Reducing host cell responses against infected cells qualifies as reducing the host's inflammatory response.

- Applicant also argues that Bout does not disclose the location and orientation of the insertion of the retained E3 sequences.
    - In response, although Bout does not explicitly disclose the position or orientation of the sequences that encode the retained E3 sequences, the deletion of some portions of the E3 region would leave the desired portions in their original position: in sense orientation.

Therefore, claims 22, 25, 27-30 and 38 are anticipated by Bout because the amended claim language does not further limit the claims or distinguish over the art.

Claim Rejections - 35 USC § 103

5. Claims 23 and 24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied above and further in view of Krajcsi *et al.* (*J. Virol.* 1996, 70(6):4904-4913, herein, "Krajcsi") for reasons of record. Applicant's arguments have been carefully considered, but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Bout teaches a vector comprising a complete E3 region, while the instant claims are drawn to a vector comprising a modified E3 region that retains only sequences encoding functional 14.5K and 10.4K proteins. This argument has been addressed above with regard to the 102(b) rejection over Bout (see above). Applicant also argues that Krajcsi provides no suggestion to retain the 10.4K and 14.5K E3 sequences in a vector. Specifically, Applicant argues that since Krajcsi does not offer a conclusive mechanism for the 14.7K protein and the RID complex, one would not be motivated to use just one.

- In response, Krajcsi's indication that the 14.7K protein and the RID complex presumably work independently provides a reasonable expectation of success that using the 14.7K protein without the RID complex, or vice versa, would work. Further, given Bout's teaching that the regions required for reducing host cell responses against infected cells (page 3, lines 1-29) include the RID complex (10.4K and 14.5K proteins), one would have been motivated to retain only these sequences.

- Applicant also argues that the claimed invention provides unexpected results. Applicant asserts that the insertion of the E3 gene sequences encoding the RID complex in place of the deleted adenoviral E3 region in "sense" orientation, provides a functional RID complex capable of efficiently counteracting inflammation response.
  - In response, Applicant's unexpected results are found in Bout's disclosure, which teaches that the regions required for reducing host cell responses against infected cells (page 3, lines 1-29) include the RID complex (10.4K and 14.5K proteins). Therefore, the unexpected results are anticipated by the prior art.

6. Claim 31 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied to claim 22, and further in view of Kovesdi *et al.* (US 5,851,806, herein, "Kovesdi"). Applicant's arguments have been carefully considered, but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Bout teaches a vector comprising a complete E3 region, while the instant claims are drawn to a vector comprising a modified E3 region that retains only

sequences encoding functional 14.5K and 10.4K proteins. This argument has been addressed above with regard to the 102(b) rejection over Bout (see above). Applicant also argues that Kovesdi only generally relates to multiply deficient adenoviral vectors.

- In response, Applicant has not addressed the motivation to combine Kovesdi and Bout, presented in the Office action of October 15, 2004. The motivation for combining the teachings of Kovesdi with Bout is found in Kovesdi's teaching that the deletion of multiple regions from the vector creates more space for larger gene inserts (Kovesdi, col. 7, lines 27-35). Therefore, the rejection is maintained for reasons of record.

7. Claims 32, 33, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied above and further in view of Kaplan *et al.* (US 6,100,086, herein, "Kaplan") and Kovesdi, for reasons of record. New claims 35 and 36 are included in this rejection. The claims are drawn to a recombinant adenoviral vector wherein the 14.5K and 10.4K protein are expressed as independent cistrons or as a discistron. The specification discloses that the protein expression is controlled by independent promoters (cistrons) or the same promoter (dicistron). While Bout does not specifically teach that the protein can be expressed with separate promoters or a single promoter, it is well within the skill of the ordinary artisan to express proteins with single or separate promoters. Kaplan discloses that transgene expression can be enforced by using strong promoters (col. 6, lines 8-19). One would have been motivated to use one promoter because that is required for expression, and also more than one promoter given Kaplan's teaching that strong promoters are used to enforce transgene expression. One would have had a reasonable

expectation of success that two promoters would have worked to express the two genes given Kaplans' teaching. Therefore, it would have been obvious to use one promoter or two promoters.

Applicant's arguments have been carefully considered, but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Bout teaches a vector comprising a complete E3 region, while the instant claims are drawn to a vector comprising a modified E3 region that retains only sequences encoding functional 14.5K and 10.4K proteins. This argument has been addressed above with regard to the 102(b) rejection over Bout (see above). Applicant also argues that Kovesdi only generally relates to multiply deficient adenoviral vectors. This argument has been addressed above in the rejection of claim 31 under 35 U.S.C. 103(a) (see above).
- Applicant also argues that Kaplan generally relates to recombinant adenovirus vectors retaining specific portions of the E3 and E4 regions that show persistent expression of the recombinant transgene. Applicant asserts that Kaplan's teaching to make chimeric adenovirus vectors from different serotypes is not sufficient to overcome the deficiencies of Bout and Kovesdi because of the deficiencies of Bout and Kovesdi. The asserted deficiencies of Bout and Kovesdi are addressed above, and therefore the Kaplan reference remains to be addressed by Applicant.

Therefore, claims 32 and 33 remain rejected for reasons of record over Bout in view of Kaplan and Kovesdi.

Conclusion

8. No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

SBC

Stacy B. Chen
March 24, 2005

James C. Housel 4/4/05

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